

AMENDMENTS TO THE CLAIMS

1-2. (Canceled)

3. (Previously presented) The composition of Claim 34, wherein the therapeutic, diagnostic, or prophylactic agent is a protein, peptide, nucleotide, oligonucleotide, saccharide, polysaccharide, organic molecule, or combination thereof.

4. (Previously presented) The composition of Claim 36, wherein the hydrophobic component is a synthetic vinyl hydrophobic polymer, a naturally derived polymer, a membrane disruptive peptide, or a phospholipid bilayer disrupting agent.

5-7. (Canceled)

8. (Previously presented) The composition of Claim 36, wherein the pH-sensitive linkage is an acetal, orthoester, cis-aconityl group, hydrazone, ester, Schiff base, dithioacetal, tert butyl ester, carbamate, thioester, or phosphoramidate.

9. (Previously presented) The composition of Claim 34, wherein the therapeutic, diagnostic, or prophylactic agent is coupled to either the hydrophilic or the hydrophobic component by a degradable or disruptable linkage.

10-12. (Canceled)

13. (Previously presented) The composition of Claim 36, wherein the conjugate further comprises a ligand, wherein the ligand specifically binds to a target molecule.

14. (Previously presented) The composition of Claim 34, wherein the therapeutic, diagnostic, or prophylactic agent is complexed to a component of the conjugate.

15. (Previously presented) The composition of Claim 36, wherein the pH sensitive linkage is hydrolyzed within about 30 to 60 minutes at a pH between 5.0 and 5.5.

16. (Previously presented) The composition of Claim 36 further comprising a pharmaceutically acceptable carrier for delivery of the conjugate to a cell or organelle.

17. (Previously presented) The composition of Claim 16, wherein the carrier provides for systemic delivery of the conjugate, local delivery of the conjugate, or topical delivery of the conjugate.

18. (Canceled)

19. (Previously presented) The composition of Claim 34, wherein the therapeutic, diagnostic, or prophylactic agent is an antisense nucleotide, ribozyme, ribozyme guide sequence, triplex forming oligonucleotide, or gene.

20-33. (Canceled)

34. (Previously presented) The composition of Claim 36 further comprising an agent, wherein the agent is a therapeutic, diagnostic, or prophylactic agent.

35. (Previously presented) The composition of Claim 36, wherein the hydrophobic component comprises a synthetic polymer.

36. (Currently amended) A composition for enhancing transport through an endosomal membrane, comprising a water-soluble hydrophilic conjugate having a hydrophobic component linked to a hydrophilic component by a pH-sensitive linkage, wherein the pH-sensitive linkage is stable at a pH between 6.8 and 8 and hydrolyzed at a pH less than 6.5 to

release the hydrophobic component, wherein the hydrophilic component comprises a polyalkylene oxide, wherein the hydrophobic component is a vinyl polymer, and wherein the hydrophobic component is an endosomal membrane disruptive ~~and allows enhanced~~ carboxylic acid-containing polymer that provides transport through ~~[[a]]~~ the endosomal membrane when released from the hydrophilic conjugate.

37. (Canceled)

38. (Currently amended) A water-soluble conjugate, comprising:

(a) a hydrophobic synthetic vinyl polymer, wherein the polymer is an endosomal membrane disruptive carboxylic acid-containing polymer that provides transport through an endosomal membrane when released from the hydrophilic conjugate;

(b) a plurality of pendant hydrophilic polyalkylene oxide components; and

(c) a plurality of pH-sensitive linkages, wherein each of the pendant polyalkylene oxide components is covalently linked to the polymer through a pH-sensitive linkage that is stable at a pH between 6.8 and 8 and hydrolyzed at a pH less than 6.5.

39. (Previously presented) The conjugate of Claim 38, wherein the synthetic vinyl polymer is a terpolymer of dimethylaminoethyl methacrylate, butyl methacrylate, and styrene benzaldehyde.

40. (Previously presented) The conjugate of Claim 38, wherein the pH-sensitive linkage is selected from the group consisting of an acetal, a dithioacetal, an ester, an orthoester, and a carbamate.

41. (Currently amended) A composition, comprising:

(a) a water-soluble hydrophilic conjugate comprising:

(i) a hydrophobic synthetic vinyl polymer, wherein the polymer is an endosomal membrane disruptive carboxylic acid-containing polymer that provides transport through an endosomal membrane when released from the hydrophilic conjugate;

(ii) a plurality of pendant hydrophilic polyalkylene oxide components;
and

(iii) a plurality of pH-sensitive linkages, wherein each of the pendant polyalkylene oxide components is covalently linked to the polymer through a pH-sensitive linkage that is stable at a pH between 6.8 and 8 and hydrolyzed at a pH less than 6.5; and

(b) a therapeutic, [[or]] diagnostic, or prophylactic agent.

42. (Previously presented) The composition of Claim 41, wherein the synthetic vinyl polymer is a terpolymer of dimethylaminoethyl methacrylate, butyl methacrylate, and styrene benzaldehyde.

43. (Previously presented) The composition of Claim 41, wherein the pH-sensitive linkage is selected from the group consisting of an acetal, a dithioacetal, an ester, an orthoester, and a carbamate.

44. (Currently amended) The composition of Claim 41, wherein the therapeutic, [[or]] diagnostic, or prophylactic agent is selected from the group consisting of a protein, a peptide, a saccharide, a polysaccharide, an organic molecule, a nucleotide, an antisense nucleotide, an oligonucleotide, a ribozyme, a ribozyme guide sequence, a triplex forming oligonucleotide, and a gene.

45. (Previously presented) The composition of Claim 36, wherein the hydrophobic component comprises a random, block, or graft copolymer, wherein the copolymer comprises an alkyl substituted or unsubstituted acrylate group.

46. (Previously presented) The composition of Claim 36, wherein the hydrophobic component comprises poly(ethylacrylic acid), poly(propylacrylic acid), poly(butylacrylic acid), or acrylic acid polymer and copolymers.

47. (Currently amended) A composition for enhancing transport through an endosomal membrane, comprising a water-soluble hydrophilic conjugate having a hydrophobic component linked to a hydrophilic component by a pH-sensitive linkage,

wherein the pH-sensitive linkage is stable at a pH between 6.8 and 8 and hydrolyzed at a pH less than 6.5 to release the hydrophobic component;

wherein the hydrophilic component comprises a polyalkylene oxide;

wherein the hydrophobic component comprises a random, block, or graft copolymer, wherein the copolymer comprises an alkyl substituted or unsubstituted acrylate group; and wherein the hydrophobic component is an endosomal membrane disruptive and allows enhanced carboxylic acid-containing polymer that provides transport through [[a]] the endosomal membrane when released from the hydrophilic conjugate.

48. (New) The composition of Claim 36, wherein the hydrophobic component is a copolymer prepared from monomers selected from the group consisting of ethylacrylic acid, propylacrylic acid, and butylacrylic acid.

49. (New) The composition of Claim 48, wherein the copolymer is prepared from monomers further comprising acrylic acid, alkyl-substituted methacrylates, or styrene.

50. (New) The composition of Claim 48, wherein the copolymer is prepared from monomers further comprising butyl methacrylate or styrene.

51. (New) The composition of Claim 48, wherein the copolymer is prepared from monomers further comprising cationic monomers.

52. (New) The composition of Claim 36, wherein the hydrophobic component is a vinyl polymer prepared from copolymerization of monomers comprising (i) monomers comprising carboxylic acid groups, (ii) cationic monomers, and (iii) hydrophobic monomers selected from the group consisting of alkyl-substituted acrylates or methacrylates, and styrene.

53. (New) The composition of Claim 34, wherein the therapeutic, diagnostic, or prophylactic agent is a nucleotide or nucleoside.

54. (New) The composition of Claim 34, wherein the therapeutic, diagnostic, or prophylactic agent is an oligonucleotide.

55. (New) The composition of Claim 34, wherein the therapeutic, diagnostic, or prophylactic agent is an RNA oligonucleotide.